

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

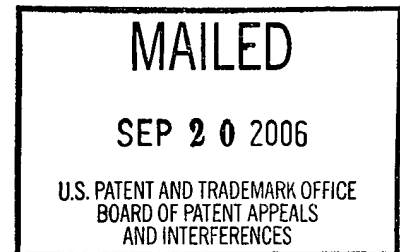
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte ISMAT ULLAH, and
NEMICHAND B. JAIN

Appeal No. 2006-2471
Application No. 09/824,364

ON BRIEF



Before SCHEINER, GRIMES, and LEOVITZ, Administrative Patent Judges.

LEOVITZ, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to methods of treating patients by administering a pharmaceutical composition containing statin and aspirin. The examiner has rejected the claims as obvious over prior art. We have jurisdiction under 35 U.S.C. § 134.

We affirm.

Background

Statins are a class of cholesterol lowering agents which are HMG CoA reductase inhibitors. Specification, page 6, lines 6-7. Examples include atorvastatin (Lipitor®) and pravastatin (Pravachol®). Id., page 7-11.

The use of aspirin for reducing the risk of a myocardial infarction and the use of statins for lowering cholesterol and preventing or treating atherosclerosis and cardiovascular disease and cerebrovascular disease are well documented. In fact, it is not uncommon that patients having elevated cholesterol levels who are at high risk for a myocardial infarction take both a statin and aspirin. However, use of both a statin and aspirin may require special care to insure that drug interaction, including physical and chemical incompatibility, and side effects, are kept to a minimum while achieving maximum benefit from these drugs.

Specification, page 1, lines 14-25.

The application provides pharmaceutical compositions to reduce the interaction of aspirin with the statin.

Discussion

Claim construction

Claims 36, 38-40, and 42-47 are on appeal. The claims stand or fall together because Appellants did not provide separate reasons for patentability of any of the claims. We select claim 46, the only independent claim, as representative. It reads as follows:

46. A method for lowering serum cholesterol or inhibiting or treating atherosclerosis or reducing risk of or treating a cardiovascular event or disease, coronary artery disease or cerebrovascular disease, which comprises administering to a patient in need of treatment a therapeutically effective amount of a pharmaceutical composition comprising a combination of a statin cholesterol lowering agent and aspirin in a single dosage form, which dosage form reduces interaction between the statin and the aspirin, wherein the pharmaceutical composition is in the form of a tablet or capsule containing both aspirin granules and statin granules.

The claim requires administering statin and aspirin in a “single dosage form.”

The application discloses tablets and capsules as examples of a single dosage form in

which the statin and aspirin are present in the same unit. Specification, page 2, line 34- page 3, line 1; page 5, line 35.

The dosage form is required by the claim to reduce “interaction between the statin and the aspirin.” According to the specification, the combined use of aspirin and a statin “may require special care” because of physical and chemical incompatibility. Id., page 1, lines 21-25. Statins are alkali salts and aspirin is acid. Id., page 1, lines 26-29. Mixing the two together “could result” in aspirin hydrolysis and statin degradation. Id., lines 28-34. In this context, we understand the term “interaction” to mean combining the statin and aspirin in such a way that could cause either of the drugs to be damaged or destroyed.

The specification does not provide a definition of what structures or other means are required by the claim to reduce the interaction between the two drugs, but it provides several examples of how this is achieved. These include, a bilayered tablet in which the drugs are segregated into different layers (id., page 3, lines 1-10), a cored tablet where one drug is present in the core and the other is contained in an outer layer (id., page 3, lines 14-21), and granular mixtures where at least one drug is granular and separately coated, e.g., with a polymer (id., page 3, line 29-page 4, line 2; page 4, line 20-page 5, line 3). In all three cases, the “dosage form” lessens direct contact between the alkaline statin and acidic aspirin as they exist together in the single formulation, thereby reducing the chance of drug damage.

Although claims must be read in view of the specification, we must be careful not to import limitations from the specification into the claims. Texas Digital Sys., Inc. v. Telegenix, Inc., 308 F.3d 1193, 1204, 64 USPQ2d 1812, 1819 (Fed. Cir. 2002). Our

mandate is to give claims “their broadest reasonable interpretation consistent with the specification.” In re Bond, 910 F.2d 831, 833, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990).

With these guiding principles, we interpret the property that the pharmaceutical composition “reduces interaction between the statin and the aspirin” to require that contact between the two drugs is reduced in the single formulation, or as they dissolve from it, for the purpose of preventing the drugs from damaging each other.

Obviousness under 35 U.S.C. § 103(a)

Claims 36, 38-40, and 42-47 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Eisman¹ in view of Eichel,² Hodges,³ and Shell.⁴

Eisman describes combinations of drugs for treating peripheral atherosclerotic disease and intermittent claudication. Eisman, Abstract. Several different drug combinations are disclosed, including a cholesterol lowering drug which is an inhibitor of the enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) and a second drug for lowering cholesterol. Id., Abstract; column 7, lines 40-55. Also disclosed are combinations that contain inhibitors of angiotensin converting enzyme and squalene synthetase. Id. The statins pravastatin and lovastatin are stated to be suitable HMG CoA inhibitors. Id., column 8, lines 56-64; column 13, lines 18-20. Aspirin is a member of a list of more than a dozen other agents which can be utilized as cholesterol lowering

¹ Eisman et al. (Eisman), U.S. Statutory Invention Registration No. H1286, published Feb. 1, 1994

² Eichel et al. (Eichel), U.S. Pat. No. 5,238,686, issued Aug. 24, 1993

³ Hodges et al. (Hodges), U.S. Pat. No. 5,225,202, issued Jul. 6, 1993

⁴ Shell et al. (Shell), U.S. Pat. No. 5,972,389, issued Oct. 26, 1999

agents in combination with the HMG CoA inhibitor. Id., column 13, lines 25-54, especially line 42.

The subject matter of the Shell patent involves “erodible, gastric-retentive drug” delivery formulations. Shell, column 1, lines 45-50. Polymers are utilized which swell as a result of imbibing water from the gastric fluid. These slowly erode, allowing the formulation to slowly deliver drug on a continuous basis to the stomach and small intestine. Id., column 1, lines 55-63; column 4, lines 28-43. Shell teaches that two or more drugs can be co-administered in the same dosage unit, where each drug is separately formulated with a polymer composition. Id., column 9, line 48-column 10, line 15. This permits multiple drugs having different half-lives to be administered, while delivering the correct dosage for each. Id.

Eichel was relied on for its teaching of enteric-coated aspirin. Eichel, Abstract. The aspirin can be granular. Id., column 5, line 65. Enteric-coated pravastatin is disclosed in Hodges. Hodges, column 6, line 55.

In setting forth the grounds of the rejection, the examiner stated that the claimed combination of a statin and aspirin was taught by Eisman. Answer, page 3. According to the examiner, Eisman also described placing drugs into a single dosage unit. Id., page 5. The motivation to have utilized the dosage form described in Shell was to control the release of each drug in order to accommodate their different half-lives. Id., page 4.

Appellants argued that the Eisman patent does not “disclose or suggest employing a statin and aspirin in the same dosage form.” Brief, page 7, lines 5-6 and 10-11. Shell was urged to be irrelevant since it did not teach the claimed combination

or that its “controlled release composition using special polymers” would result in a pharmaceutical that reduced the interaction of statin with aspirin. Id., page 8, paragraph 7.

“When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness.” In re Sang Su Lee, 277 F.3d 1338, 1343, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002). We focus on the Eisman and Shell patents since these formed the core of the rejection.

Appellants did not contest that the use of a statin and aspirin in separate dosage units would have been obvious to one of ordinary skill in the art. In the application, they appeared to admit that the combination had been used in the prior art to treat patients.

The use of aspirin for reducing the risk of a myocardial infarction and the use of statins for lowering cholesterol and preventing or treating atherosclerosis and cardiovascular disease and cerebrovascular disease are well documented. In fact, it is not uncommon that patients having elevated cholesterol levels who are at high risk for a myocardial infarction take both a statin and aspirin.

Specification, page 1, lines 14-20; see also, Brief, page 4, paragraph 4.

Instead, Appellants urged that Eisman’s deficiency was its failure to disclose or suggest a single dosage form containing both a statin and aspirin. Brief, page 7. Thus, the obviousness issue boils down to whether one of ordinary skill in the art would have been motivated to have combined the two claimed ingredients into a single dosage form that “reduces interaction between the statin and the aspirin.” As evidence that motivation existed, the examiner pointed to disclosures in both Eisman and Shell.

Eisman states that the “cholesterol lowering agent and ACE inhibitor may be employed together in the same dosage form or in separate oral dosage forms, which may be taken at the same time.” Eisman, column 15, lines 60-63. A statin (required by instant claim 47) is disclosed as an example of a drug (an inhibitor of HMG CoA reductase) that lowers cholesterol. Id., column 7, lines 43-46; column 8, line 56-65; column 22, claims 2, 3, and 10. The indication is for atherosclerotic diseases or intermittent claudication. Id., column 7, lines 40-45. This is the same indication recited in claim 47.

Next, the examiner introduced Shell as evidence. Shell describes drug combinations that contain two or more drugs in the same dosage form. Shell, column 9, lines 48-52. As an example, the combination of an ACE inhibitor plus a diuretic is disclosed. Id., column 10, lines 16-24. The patent states these “particular combinations are useful in cardiovascular medicine, and provide advantages of reduced cost over separate administrations of the different drugs, plus the particular advantage of reduced side effects and enhanced patient compliance.” Id., column 10, lines 25-30.

There is no explicit teaching that a statin and aspirin be formulated together. However, both Eisman and Shell put two drugs into the same dosage unit to treat a cardiovascular indication, the same field of treatment as claimed here. In Eisman, one of these drugs is a cholesterol-lowering drug, the same class of compounds recited in the instant claims. Together, these establish that the concept of combining cardiovascular drugs, including a cholesterol-lowering drug, in a single dosage form was known prior to the application filing date. Shell puts into words reasons for it: to reduce cost, to reduce side effects, and to increase patient compliance. Shell, column 10, lines

25-30. In our view, the skilled worker – knowing that statins and aspirin are used to treat cardiovascular diseases – would have recognized the advantages of placing the two together in a single unit, as done for other cardiovascular drugs, and would have been motivated to have done so with these. A suggestion, teaching, or motivation to combine the relevant prior art teachings does not have to be found explicitly in the prior art, but may be implicit from the prior art as a whole. In re Kahn, 441 F.3d 977, 987-88, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

In addition to combining the two drugs in the same unit, Shell also explains why each drug would be separately mixed with its own carrier.

Different drugs have different biological half-lives which determine their required frequency of administration (once daily, four times daily, etc.). Thus, when two or more drugs are co-administered in one conventional medication unit, an unfavorable compromise is often required, resulting in an underdose of one drug and an overdose of the other. One of the advantages of the dosage forms of the present invention is that they can be used to deliver multiple drugs without requiring such compromises. For example, in an alternative embodiment, a plurality of drug-containing, spherical, spheroidal- or cylindrical-shaped particles are provided, some of the particles containing a first drug/polymer composition designed to release the first drug at its ideal rate and duration (dose), while other particles contain a second drug/polymer composition designed to release the second drug at its ideal rate and duration.

Column 9, lines 48-63.

Appellants did not explain why the aforementioned disclosures in Eisman and Shell were inadequate to provide motivation to establish prima facie obviousness of the claimed subject matter. Appellants stated that Shell was “totally different” from the claimed subject matter because it was “not concerned with using a statin and aspirin in the same dosage form.” Brief, page 8, paragraph 7. However, the examiner did not rely on Shell for teaching the statin/aspirin combination.

Appellants also contended that there was “no disclosure or suggestion ... that the polymer of Shell et al. could prevent or reduce interaction between aspirin and statin.” Brief, page 9, lines 29-32. We do not find this argument persuasive. Reduction in the interaction between statin and aspirin would reasonably be presumed to be a consequence of following Shell’s disclosure of formulating each drug with its own carrier. Our construction of claim 46 would cover this embodiment taught by Shell. The fact that Appellants may have recognized an advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the difference would otherwise have been obvious. Ex parte Obiaya, 227 USPQ 58, 60 (BPAI 1985), *aff’d*.mem., 795 F.2d 1017 (Fed. Cir. 1986). Appellants have not articulated why the claimed property requiring a reduced “interaction between the statin and aspirin” would not naturally flow from Shell’s teachings.

In sum, Appellants’ arguments did not squarely address the examiner’s point that Shell provides adequate motivation to have combined a statin and aspirin in a single dosage form having the claimed features.

Appellants’ primary argument centered on the “incompatibility” of statin and aspirin. However, Appellants appear to admit this fact was known prior to the application filing date.

However, use of both a statin and aspirin in a single dosage form could result in drug interaction, which could result in physical and chemical incompatibility, leading to a reduction in benefit derived from these drugs. Accordingly, in the past, patients on both statin and aspirin have taken these drugs in separate dosage forms.
Brief, page 4.

At best, one skilled in the art reading Eisman et al., knowing that a statin and aspirin unfavorably interact, absent the use of hindsight in view of

Appellants' disclosure, would employ the statin and aspirin in separate dosage forms.

Id., page 7.

Eisman et al. do not teach or suggest a single dosage form containing both a statin and aspirin since it was known that the statin and aspirin would interact to reduce efficacy of each.

Id., page 11.

Were it known that statin and aspirin were incompatible as alleged by Appellants, Shell provides motivation to have utilized its controlled release dosage forms.

According to Shell, "drugs that are otherwise chemically incompatible when formulated together can be delivered simultaneously via separate swellable particles contained in a single dosage form." Shell, column 10, lines 47-51. This is a clear case where the "suggestion to combine references may flow from the nature of the problem."

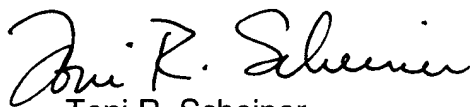
Kahn, 441 F.3d at 988, 78 USPQ2d at 1337. For this reason, we do not see how Appellants' argument helps their case. Nonetheless, even if the co-stability problem had not been recognized in the prior art, the advantages described by Shell for its dual drug formulations (release each drug at its optimal rate and duration; improved compliance, reduce side-effects, etc.) are sufficient to establish a case of prima facie obviousness. On the record before us, we do not find that Appellants provided sufficient arguments to rebut it. This rejection is affirmed. All pending claims fall together since separate reasons for patentability were not provided.

Summary

The rejection of the claims over prior art is affirmed.

No time period for taking any subsequent action in connection with this appeal
may be extended under 37 CFR § 1.136(a).

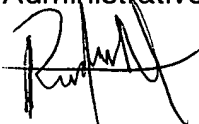
AFFIRMED



Toni R. Scheiner
Administrative Patent Judge



Eric B. Grimes
Administrative Patent Judge



Richard M. Lebovitz
Administrative Patent Judge

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